Advanced Synthesis & Catalysis

Accepted Article

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To be cited as: *Adv. Synth. Catal.* 10.1002/adsc.201700462

Link to VoR: http://dx.doi.org/10.1002/adsc.201700462

10.1002/adsc.201700462

COMMUNICATION

DOI: 10.1002/adsc.201((will be filled in by the editorial staff))

Synthesis of 1-Vinyl/Aryl Benzotriazole 3-Oxides through Copper-Mediated C-N Bond Coupling Reaction

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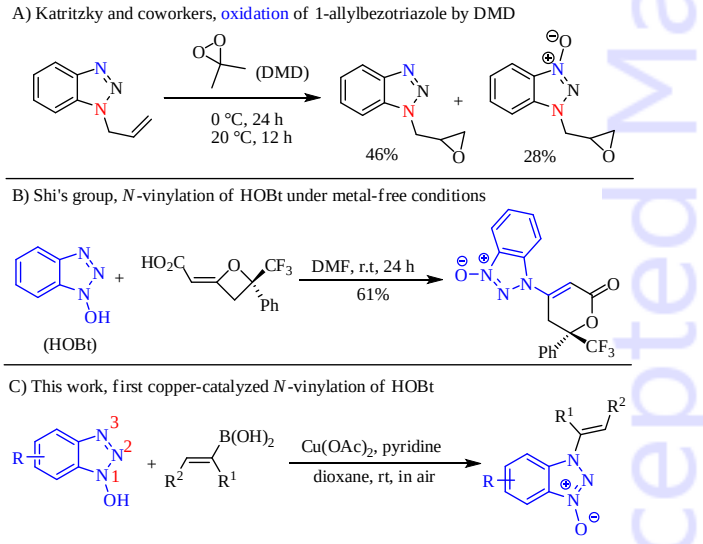
Received: ((will be filled in by the editorial staff))

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/adsc.201######.((Please delete if not appropriate))

Abstract: An efficient synthesis of 1-vinyl/aryl benzotriazole 3-oxides via the copper-promoted coupling of *N*-hydroxybenzotriazoles with alkenyl or aryl boronic acids is reported. This strategy features mild reaction conditions, good functional group tolerance, broad substrate scope and rapid introduction of benzotriazole *N*-oxides moieties into molecules. Density functional theory calculations revealed that the formation of the favored *N*-coupling product depends on the kinetically more favorable C−N bond formation pathway.

Keywords: copper-catalyzed; organoboronic acids; C−N bond formation; benzotriazole oxides; N−O bond compounds

1-Vinyl benzotriazole derivatives have a broad range of biological activity[1] such as tubulin inhibition[1a] or anti-inflammatory properties[1b], and are extensively used as versatile synthetic intermediates.[2] Some studies show that *N*-oxide groups exhibit better bioactivity than their parent heterocycles in pharmaceuticals.[3] Thus, modification of 1-vinyl benzotriazoles to 1-vinyl benzotriazole *3*-oxides is desirable for further applications in pharmaceutical and medicinal chemistry. Traditional syntheses of *N*-oxides involve direct oxidation of the nitrogen with oxidants such as *m*-CPBA, oxone, or H_2O_2,[4] but direct oxidation is not suitable for benzotriazoles containing a vinyl bond. For example, Katritzky and co-workers found that 1-allylbenzotriazole was preferentially oxidized at the C=C bond by dimethyldioxirane (DMD), giving a mixture of oxidation products (Scheme 1-A).[5] In 2012, Shi and co-workers reported that 1-vinyl benzotriazole *3*-oxide could be prepared through Michael addition of *N*-hydroxybenzotriazole to oxetane under metal-free conditions at room temperature, but only one example was reported (Scheme 1-B).[6] Consequently, the synthesis of 1-vinyl benzotriazole *3*-oxides remains challenging, and a general and practical strategy to access these compounds is desirable.



Scheme 1. Strategies to prepare 1-vinyl benzotriazole 3-oxides.

Oxidative cross-coupling has been identified as a promising strategy for the construction of carbon-heteroatom bonds.[7] Direct *N*-functionalization of the N−O bond can be used to synthesize *N*-oxide derivatives, such as quinoline and pyridine *N*-oxides,[8] and nitrones.[9] *N*-Hydroxybenzotriazole (HOBt) is a widely used N-O bond compound, serving as an activating reagent in organic and peptide syntheses.[10] In transition-metal catalyzed reactions of *N*-hydroxybenzotriazole with diverse coupling reagents, the *O*-atom has primarily acted as

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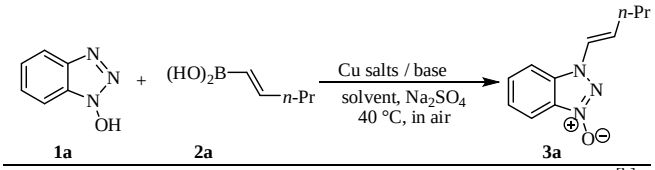
a nucleophilic site, while the *N*-atom has rarely served as a nucleophilic site.[11] During studies on *O*-arylation of the N-O bond in our group,[12] we surmised that direct coupling of the N^3 atom in HOBt with alkenyl boronic acids under a copper-mediated reaction to provide *N*-vinyl benzotriazole oxides would be possible (Scheme 1-C).[13] Herein, we report a coupling strategy to synthesize 1-vinyl benzotriazole 3-oxides in high yields and broad substrate scope.

Initially, the direct *N*-vinylation by a copper catalyst was optimized. When HOBt (**1a**) and alkenyl boronic acid (**2a**) were added with 1.0 equiv of $CuSO_4$, Na_2SO_4 (6.0 equiv) and 10 equiv of pyridine (pyr) in 1,2-dichloroethane (DCE) at 40 °C under air, the desired product **3a** was obtained in 30% yield (Table 1, entry 1). The reaction did not occur with $CuCl_2$ or CuBr, but afforded **3a** in 40% and 80% yields with CuI and Cu_2O, respectively (Table 1, entries 2-5). Product **3a** was obtained 90% yield by using $Cu(OAc)_2$ as a catalyst (Table 1, entry 6). The yield of **3a** decreased to 82% without Na_2SO_4 in DCE (Table 1, entry 7). Solvent screening showed that the best result was obtained in dioxane (Table 1, entries 8−13). However, the yield of **3a** also dropped without Na_2SO_4 (Table 1, entry 14). The amount of $Cu(OAc)_2$ and pyridine also affected the yields of **3a** (Table 1, entries 15−17). For example, the yield of **3a** decreased to 73% when the amount of $Cu(OAc)_2$ was reduced to 0.2 equiv. Using 5.0 equiv of pyridine provided **3a** in 82% yield. The nature of the base was also important for the *N*-vinylation process (Table 1, entries 18−20). No reaction took place when using Cs_2CO_3, but organic bases did promote the reaction. The optimal reaction conditions were 1.0 equiv of $Cu(OAc)_2$ and 10 equiv of pyridine in dioxane under an air atmosphere (Table 1, entry 13).

Table 1. Optimization of the Reaction Conditions. [a]



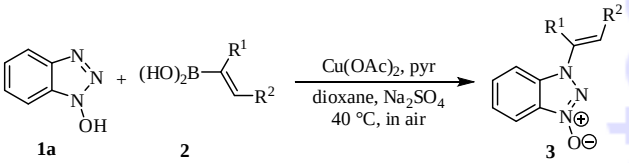
1a **2a** **3a**

Entry	Cu salts	Equiv	Solvent	Base	**3a** %[b]
1	$CuSO_4$	1.0	DCE	pyr	30
2	$CuCl_2$	1.0	DCE	pyr	0
3	CuBr	1.0	DCE	pyr	0
4	CuI	1.0	DCE	pyr	41
5	Cu_2O	1.0	DCE	pyr	80
6	$Cu(OAc)_2$	1.0	DCE	pyr	90
7	$Cu(OAc)_2$	1.0	DCE	pyr	82[c]
8	$Cu(OAc)_2$	1.0	DCM	pyr	71
9	$Cu(OAc)_2$	1.0	toluene	pyr	85
10	$Cu(OAc)_2$	1.0	THF	pyr	65
11	$Cu(OAc)_2$	1.0	MeCN	pyr	84
12	$Cu(OAc)_2$	1.0	DMF	pyr	86
13	$Cu(OAc)_2$	1.0	dioxane	pyr	96
14	$Cu(OAc)_2$	1.0	dioxane	pyr	84[c]
15	$Cu(OAc)_2$	0.2	dioxane	pyr	73
16	$Cu(OAc)_2$	0.5	dioxane	pyr	85
17	$Cu(OAc)_2$	1.0	dioxane	pyr	82[d]
18	$Cu(OAc)_2$	1.0	dioxane	Cs_2CO_3	<5
19	$Cu(OAc)_2$	1.0	dioxane	Et_3N	73
20	$Cu(OAc)_2$	1.0	dioxane	bipyr	59

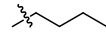
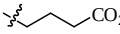
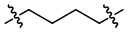
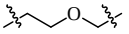
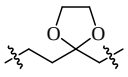
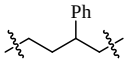
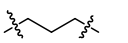
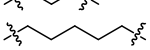
[a] Reaction conditions: **1a** (0.2 mmol), **2a** (0.6 mmol, 3.0 equiv), Cu salts (1.0 equiv), base (10.0 equiv), solvent (2 mL), Na_2SO_4 (6 equiv), 40 °C, 18−24 h. [b] Isolated yield; [c] Without Na_2SO_4; [d] Pyridine (5.0 equiv).

Using the optimized conditions, we examined the substrate scope of the reaction for alkenyl boronic acids. As shown in Table 2, terminal linear and branched alkyl-substituted, *Z*-disubstituted, and cyclic alkenyl boronic acids could be converted to products **3** in good to excellent yields. The geometry of the alkenyl boronic acids was retained in the products. Alkenyl boronic acids containing sensitive chloro, ester, and ketal functional groups smoothly underwent *N*-vinylation in high yields. The reaction was compatible with cyclic alkenyl boronic acids with five, six, and seven-membered rings, but a low yield was obtained for the seven-membered ring (Table 2, entries 9-14). Interestingly, 0.2 equiv of copper also provided **3i** in good yields (Table 2, entries 1−3, 5−6, 9, and 13). The yield for some products **3** was low because the substrate **1** could not be consumed completely (Table 2, **3e**, **3h** and **3n**). In no case the *O*-arylation products was observed. The structure of product **3** was confirmed by X-ray diffraction analysis of compound **3l** (see Figure 1).[14] The broad scope of this coupling reaction of HOBt **1a** and alkenyl boronic acids **2** provides a good starting point for the synthesis of other benzotriazole oxides.

Table 2. Substrate Scope of Alkenyl Boronic Acids. [a]



1a **2** **3**

entry	**2**	R^1	R^2	**3**	yield %[b]
1	**2a**	H	*n*-Pr	**3a**	96 (84)[c]
2	**2b**	H	*n*-Bu	**3b**	89 (78)[c]
3	**2c**	H		**3c**	80 (60)[c]
4	**2d**	H		**3d**	82
5	**2e**	H	4-$MeOC_6H_5$	**3e**	65 (55)[c]
6	**2f**	H	4-FC_6H_5	**3f**	73 (52)[c]
7	**2g**	Me	Me	**3g**	73
8	**2h**	Ph	Et	**3h**	37
9	**2i**			**3i**	62 (70)[c]
10	**2j**			**3j**	67
11	**2k**			**3k**	58
12	**2l**			**3l**	66
13	**2m**			**3m**	73 (67)[c]
14	**2n**			**3n**	32

[a] Reaction conditions: **1a** (0.3 mmol), **2** (0.9 mmol, 3.0 equiv), $Cu(OAc)_2$ (0.3 mmol, 1.0 equiv), Na_2SO_4 (6 equiv),

pyr (3.0 mmol, 10.0 equiv), dioxane (3 mL), 40 °C, 18−24 h. [b] Isolated yield; [c] 0.2 equiv $Cu(OAc)_2$.

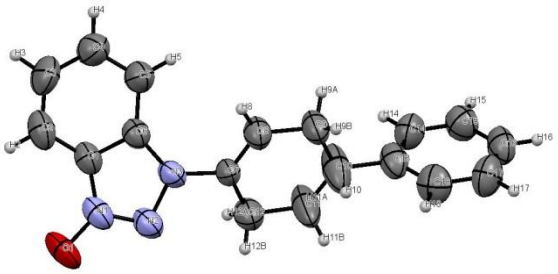
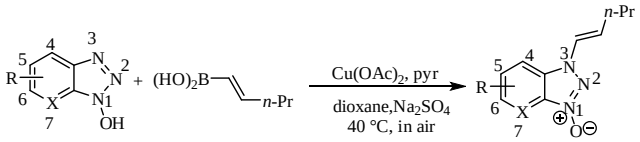


Figure 1. Crystal structure of compound **3l**.

This oxidative coupling reaction can also be applied to other *N*-hydroxybenzotriazoles **1**. *N*-Vinylation was successful for compounds with electron-donating and electron-withdrawing groups in the 5- and 6-positions of the aryl ring. However, when a chloro substituent was present in the 4-position, the yield of **3ah** was reduced to 23% with recovery of **1h**. This incomplete reaction might be a consequence of the steric hindrance in the 4-position close to the N^3 atom (Table 3, entry 8). 7-Aza-3-hydroxybenzotriazole **1i** gave the desired product **3ai** in 57% yield (Table 3, entry 9).

Table 3. Substrate Scope of *N*-Hydroxybenzotriazoles **1**.[a]



1 **2a** **3ab-3ai**

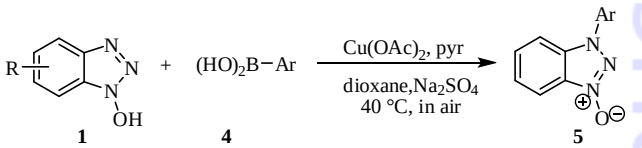
X = C (**1a-1h**), N (**1i**)

Entry	**1**	R	**3**	Yield (%)[b]
1	**1a**	H	**3a**	95
2	**1b**	6-MeO	**3ab**	68
3	**1c**	6-Me	**3ac**	77
4	**1d**	6-Cl	**3ad**	77
5	**1e**	6-CF_3	**3ae**	80
6	**1f**	6-CN	**3af**	76
7	**1g**	5-Me	**3ag**	89
8	**1h**	4-Cl	**3ah**	23
9	**1i**	H	**3ai**	57

[a] Reaction conditions: **1** (0.3 mmol), **2a** (0.9 mmol, 3.0 equiv), $Cu(OAc)_2$ (0.3 mmol, 1.0 equiv), Na_2SO_4 (6 equiv), pyr (3.0 mmol, 10.0 equiv), dioxane (3 mL), 40 °C, 18−24 h. [b] Isolated yield.

The copper-mediated coupling reaction is not only suitable for *N*-vinylation, but can also be used for *N*-arylation with arylboronic acids **4**. These results are summarized in Table 4. Various electron-rich and electron-deficient groups with *ortho*-, *meta*-, and *para*-substituents were efficiently arylated to afford 1-aryl benzotriazole 3-oxides **5** in high yields. Substrates with electron-rich groups generally gave better yields than those with electron-deficient groups (Table 4, entries 2–6 *vs* 8–10). Heteroaryl boronic acids such as 2-thienyl and 5-indolyl boronic acids gave the corresponding products only in moderate yields (Table 4, entries 14–15). Interestingly, good yields of product **5** were still obtained using a catalytic $Cu(OAc)_2$ for some arylboronic acids (Table 4, entries 3, 6, 7, 9, and 14). Lam and co-workers reported a copper-mediated coupling reaction of HOBt and 4-methylphenyl boronic acids and the *O*-coupling product was afforded in 44% yield. However, there was no data characterizing the *O*-coupling product and they did not mention the *N*-coupling products.[15] When we repeated the conditions used by Lam's group, only the *N*-arylation product was obtained and the structure was confirmed by X-ray diffraction of compound **5h** (see Figure 2).[16]

Table 4. Substrate Scope of Arylboronic Acids.[a]



1 **4** **5**

Entry	**1**	Ar	**5**	Yield (%)[b]
1	**1a**	Ph	**5a**	77(58)[c]
2	**1a**	4-$MeOC_6H_4$	**5b**	95(82)[c]
3	**1a**	4-$PhOC_6H_4$	**5c**	77(92)[c]
4	**1a**	4-$MeSC_6H_4$	**5d**	85(66)[c]
5	**1a**	4-$(Me)_2NC_6H_4$	**5e**	80(18)[c]
6	**1a**	4-MeC_6H_5	**5f**	80(85)[c]
7	**1a**	4-$(CH_2{=}CH)C_6H_4$	**5g**	49(70)[c]
8	**1a**	4-FC_6H_4	**5h**	73(73)[c]
9	**1a**	4-$CF_3C_6H_4$	**5i**	62(66)[c]
10	**1a**	4-$CHOC_6H_4$	**5j**	43(46)[c]
11	**1a**	3-$MeOC_6H_4$	**5k**	80(30)[c]
12	**1a**	3,5-$Me_2C_6H_3$	**5l**	79(75)[c]
13	**1a**	2-naphthyl	**5m**	68(65)[c]
14	**1a**	2-thienyl	**5n**	35(66)[c]
15	**1a**	5-indolyl	**5o**	61(27)[c]
16	**1b**	Ph	**5p**	60
17	**1e**	Ph	**5q**	71

[a] Reaction conditions: **1** (0.3 mmol), **4** (0.9 mmol, 3.0 equiv), $Cu(OAc)_2$ (0.3 mmol, 1.0 equiv), Na_2SO_4 (6 equiv), pyr (3.0 mmol, 10.0 equiv), dioxane (3 mL), 40 °C, 18−24 h; [b] Isolated yield; [c] 0.2 equiv $Cu(OAc)_2$.

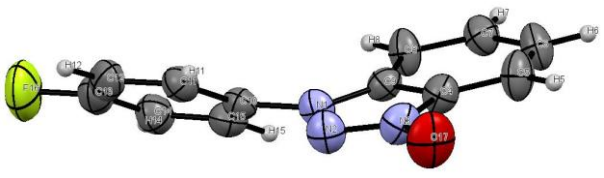


Figure 2. Crystal structure of compound **5h.**

The *O*- or *N*-arylation mechanism *via* the copper-catalyzed coupling reaction has been studied by the

Stahl,[17] Norrby,[18] and Das[19] groups by using density functional theory (DFT) calculations. The reaction involves transmetallation, binding, deprotonation, oxidation, and reductive elimination steps. A Cu (III) species was proposed as the key intermediate in these studies. In our case, the coupling reaction was not affected by addition of radical trapping reagents such as TEMPO or *p*-benzoquinone.[20]

To understand the selective *N*-arylation over *O*-arylation of *N*-hydrobenzotriazole, DFT calculations were carried out on the model reaction of HOBt **1a** with phenylboronic acid **4a**. It was shown previously that compounds **1a** and **1a'** are in equilibrium.[21] Cu (III) intermediates **IN1-O** and **IN1-N** were formed with the former only 0.2 kcal/mol lower in free energy than the latter after transmetallation, binding, deprotonation, and oxidation processes.[22] The selectivity-determining reductive elimination step proceeds through transition states **TS1-O** and **TS1-N** to release the Cu^{I}(OAc)(pyr) and form products **6a** and **5a**. Figure 3 shows that **TS1-O** is 3.0 kcal/mol less favorable than **TS1-N**, making the O–arylation pathway less likely to occur. Moreover, the formation of a more stable N–Ph product (**5a**: −39.8 kcal/mol) with respect to the O–Ph product (**6a**: −33.9 kcal/mol) is a large driving force for the *N*-arylation process.

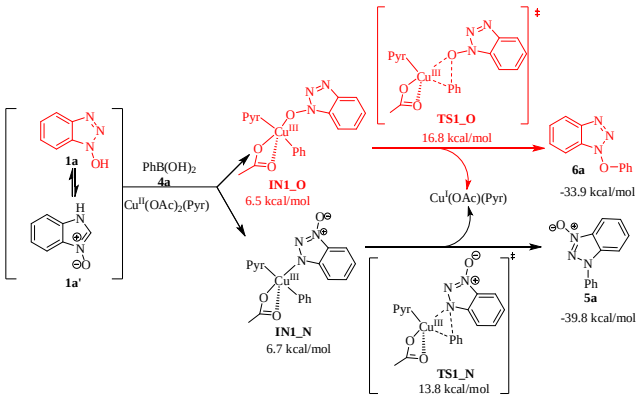
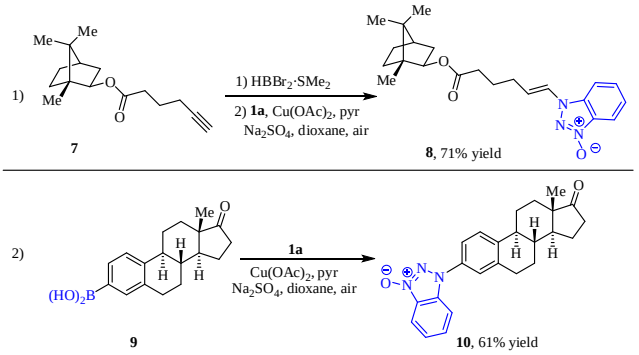


Figure 3. Energy profiles for the formation steps of the N–Ph and O–Ph products.[23]

Finally, we illustrated the utility of this new protocol for rapid introduction of the benzotriazole oxide group into more complex molecules. Treatment of alkyne **7** with $HBBr_2{\cdot}SMe_2$ and subsequent reaction with **1a** under copper-mediated conditions afforded the *N*-vinylation product **8** in 71% yield (Scheme 2-1). Estrone-derived boronic acid **9** reacted with **1a** to provide the desired product **10** in 61% yield (Scheme 2-2). These results show that further applications of this method in the synthesis of bioactive compounds are feasible.



Scheme 2. Applications of the *N*-vinylation/arylation process.

In summary, we have developed a protocol for the direct *N*-vinylation/arylation of *N*-hydroxy benzotriazoles with alkenyl or arylboronic acids to prepare 1-vinyl/aryl benzotriazole 3-oxides in good to excellent yields via the copper-mediated coupling reaction. This reaction can be used for rapid and efficient introduction of benzotriazole oxide group into molecules. The reaction provides a general and practical method to access 1-vinyl/aryl benzotriazole 3-oxides.

Experimental Section

General Procedure for Synthesis of 3a: A 25 mL flask was charged with *N*-hydroxybenzotriazole **1a** (0.041 g, 0.3 mmol), $Cu(OAc)_2$ (0.30 mmol, 1.0 equiv), anhydrous Na_2SO_4 (400 mg, 6.0 equiv) and alkenyl boronic acids **2a** (0.103 g, 0.9 mmol) in air atmosphere, dioxane (3.0 mL) and pyridine (0.25 mL, 10.0 equiv) was added *via* syringe. The reaction mixture was capped with a septum pierced with a ventilation needle and stirred vigorously at 40 °C for 15−26 h until substrate **1a** disappeared (monitored by TLC). At this time, the reaction was quenched with H_2O (10 mL) and extracted with DCM (3 × 10 mL). Then, the organic layers were combined and dried with Na_2SO_4 and filtered. The solvent was removed under reduced pressure and the crude product was purified by flash chromatography (the crude residue was dry loaded with silica gel, 1/6 to 2/1, ethyl acetate/petroleum ether) to provide product **3a**. A white solid (0.059 g, 96%). mp: 94−95 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94 (d, J = 6.8 Hz, 1H), 7.62 (t, J = 7.2 Hz, 2H), 7.39 (t, J = 6.0 Hz, 1H), 6.92 (d, J = 14.0 Hz, 1H), 6.38−6.31 (m, 1H), 2.22 (q, J = 6.8 Hz, 2H), 1.54−1.49 (m, 2H), 0.97 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 132.1, 130.7, 130.5, 124.6, 122.7, 120.3, 115.7, 110.5, 31.8, 22.3, 13.5; IR (thin film) 3073, 2956, 1601, 1496, 1424, 1378, 730 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{11}H_{14}N_3O(M+H)^+$ 204.1137, found 204.1127.

Acknowledgements

Financial support from the "Overseas 100 Talents Program" of Guangxi Higher Education, National Natural Science Foundation of China (21562005, 21602037, 21462008), and Natural Science Foundation of Guangxi (2016GXNSFFA380005) are greatly appreciated. L. Xu acknowledges PKUSZ for computational resources and Prof. Xinhao Zhang and Prof. Olaf Wiest for helpful discussions and manuscript proofreading.

References

[1] a) A. Carta, I. Briguglio, S. Piras, G. Boatto, P. La Colla, R. Lododo, M. Tolomeo, S. Grimaudo, A. Di Cristina, R. M. Pipitone, E. Laurini, M. S. Paneni, P. Posocco, M. Fermeglia, S. Pricl, *Eur. J. Med. Chem.* **2011**, *46*, 4151; b) P. Sanna, A. Carta, M. E. R. Nikookar, *Eur. J. Med. Chem.* **2000**, *35*, 535; c) K. M. Dawood, H. Abdel-Gawad, E. A. Rageb, M. Ellithey, H. A. Mohamed, *Bioorg. Med. Chem.* **2006**, *14*, 3672.

[2] a) A. R. Katritzky, S. Rachwal, *Chem. Rev.* **2010**, *110*, 1564; b) A. R. Katritzky, S. Bobrov, K. Kirichenko, Y. Ji, P. J. Steel, *J. Org. Chem.* **2003**, *68*, 5713.

[3] a) R. A. Edrada, P. Proksch, V. Wray, L. Witte, W. E. G. Müller, R. W. M. Van Soest, *J. Nat. Prod.* **1996**, *59*, 1056; b) M. Chioua, D. Sucunza, E. Soriano, D. Hadjipavlou-Litina, A. Alcázar, I. Ayuso, M. J. Oset-Gasque, M. P. González, L. Monjas, M. I. Rodríguez-Franco, J. Marco-Contelles, A. Samadi, *J. Med. Chem.* **2012**, *55*, 153; c) G. Durand, B. Poeggeler, S. Ortial, A. Polidori, F. A. Villamena, J. Böker, R. Hardeland, M. A. Pappolla, B. Pucci, *J. Med. Chem.* **2010**, *53*, 4849; d) Y. Tang, Y. Fu, J. Xiong, M. Li, G.-L. Ma, G.-X. Yang, B.-G. Wei, Y. Zhao, H.-Y. Zhang, J.-F. Hu, *J. Nat. Prod.* **2013**, *76*, 1475.

[4] a) C. Aciro, S. G. Davies, W. Kurosawa, P. M. Roberts, A. J. Russell, J. E. Thomson, *Org. Lett.* **2009**, *11*, 1333; b) C. B. Huehls, J. Huang, J. Yang, *Tetrahedron* **2015**, *71*, 3593; c) C. Matassini, C. Parmeggiani, F. Cardona, A. Goti, *Org. Lett.* **2015**, *17*, 4082; d) C. Gella, È. Ferrer, R. Alibés, F. Busqué, P. De March, M. Figueredo, J. Font, *J. Org. Chem.* **2009**, *74*, 6365.

[5] A. R. Katritzky, R. Maimait, S. N. Denisenko, P. J. Steel, N. G. Akhmedov, *J. Org. Chem.* **2001**, *66*, 5585.

[6] Q.-Y. Zhao, L. Huang, Y. Wei, M. Shi, *Adv. Synth. Catal.* **2012**, *354*, 1926.

[7] See reviews: a) C. Liu, H. Zhang, W. Shi, A. Lei, *Chem. Rev.* **2011**, *111*, 1780; b) C. Liu, D. Liu, A. Lei. *Acc. Chem. Res.* **2014**, *47*, 3459; c) C. S. Yeung, V. M. Dong, *Chem. Rev.* **2011**, *111*, 1215; d) J. J. Mousseau, A. B. Charette, *Acc. Chem. Res.* **2013**, *46*, 412.

[8] a) S. Guven, M. S. Ozer, S. Kaya, N. Menges, M. Balci, *Org. Lett.* **2015**, *17*, 2660; b) Z. Shi, D. C. Koester, M. Boultadakis-Arapinis, F. Glorius, *J. Am. Chem. Soc.* **2013**, *135*, 12204; c) D. Francois, A. Maden, W. V. Murray, *Org. Lett.* **2004**, *6*, 1931.

[9] a) R.-H. Liu, D. Wei, B. Hang, W. Yu, *ACS Catal.* **2016**, *6*, 6525; b) X.-P. Ma, W.-M. Shi, X.-L. Mo, X.-H. Li, L.-G. Li, C.-X. Pan, B. Chen, G.-F. Su, D.-L. Mo, *J. Org. Chem.* **2015**, *80*, 10098; c) X.-Y. Duan, N.-N. Zhou, R. Fang, X.-L. Yang, W. Yu, B. Han, *Angew. Chem. Int. Ed.* **2014**, *53*, 3158; *Angew. Chem.* **2014**, *126*, 3222; d) S.-Y. Wu, X.-P. Ma, C. Liang, D.-L. Mo, *J. Org. Chem.* **2017**, *82*, 3232.

[10] a) P. Wang, X. Li, J. Zhu, J. Chen, Y. Yuan, X. Wu, S. J. Danishefsky, *J. Am. Soc. Chem.* **2011**, *133*, 1597; b) M. Jiang, M. Shi, *J. Org. Chem.* **2009**, *74*, 2516; c) A. Ohkubo, Y. Kuwayama, T. Kudo, H. Tsunoda, K. Seio, M. Sekine, *Org. Lett.* **2008**, *10*, 2793.

[11] a) M. Kumar, M. Scobie, M. S. Mashuta, G. B. Hammond, B. Xu, *Org. Lett.* **2013**, *15*, 724; b) A. A. Andia, M. R. Miner, K. A. Woerpel, *Org. Lett.* **2015**, *17*, 2704.

[12] a) Z.-X. Wang, W.-M. Shi, H.-Y. Bi, X.-H. Li, G.-F. Su, D.-L. Mo, *J. Org. Chem.* **2016**, *81*, 8014; b) W.-M. Shi, X.-P. Ma, C.-X. Pan, G.-F. Su, D.-L. Mo, *J. Org. Chem.* **2015**, *80*, 11175.

[13] Some recent examples for copper-catalyzed selective *N*-vinylation, see: a) J. Ohata, M. B. Minus, M. E. Abernathy, Z. T. Ball, *J. Am. Chem. Soc.* **2016**, *138*, 7472; b) D.-L. Mo, D. A. Wink, L. L. Anderson, *Org. Lett.* **2012**, *14*, 5180; c) D. Kontokosta, D. S. Mueller, D.-L. Mo, W. H. Pace, R. A. Simpson, L. L. Anderson, *Beilstein J. Or g. Chem.* **2015**, *11*, 2097; d) Z. H. Zhang, Y. Yu, L. S. Liebeskind, *Org. Lett.* **2008**, *10*, 3005; e) S. Dalili, A. K. Yudin, *Org. Lett.* **2005**, *7*, 1161.

[14] CCDC 1534955 for compound (**3l**) contains the supplementary crystallographic data for this paper.

[15] P. Y. S. Lam, C. G. Clark, S. Saubern, J. Adams, K. M. Averill, D. M. T. Chan, A. Combs, *Synlett* **2000**, *5*, 674.

[16] CCDC 1534956 for compound (**5h**) contains the supplementary crystallographic data for this paper.

[17] a) A. E. King, T. C. Brunold, S. S. Stahl, *J. Am. Chem. Soc.* **2009**, *131*, 5044; b) A. E. King, B. L. Ryland, T. C. Brunold, S. S. Stahl, *Organometallics* **2012**, *31*, 7948.

[18] P.-F. Larsson, C.-J. Wallentin, P.-O. Norrby, *ChemCatChem* **2014**, *6*, 1277.

[19] a) A. S. Reddy, K. R. Reddy, D. N. Rao, C. K. Jaladanki, P. V. Bharatam, P. Y. S. Lam, P. Das, *Org. Biomol. Chem*. **2017**, *15*, 801; b) K. A. Kumar, P. Kannaboina, C. K. Jaladanki, P. V. Bharatam, P. Das, *ChemistrySelect* **2016**, *3*, 601.

[20] To verify the radical process of the coupling reaction, some radical trapping reagents were used. Please see the detailed results in the Supporting Information.

[21] B. D. Brink, J. R. DeFrancisco, J. A. Hillner, B. R. Linton, *J. Org. Chem.* **2011**, *76*, 5258.

[22] a) Our calculation of key Cu^{III} species with the binding of one pyridine ligand is at least 2.6 kcal/mol more favorable than that without binding; b) The triplet spin states for the Cu^{III} species are also quite unstable compared with the singlet spin states. A possible catalytic cycle for the *N*-coupling mechanism was proposed, for details see Scheme S2 in Supporting Information.

[23] Geometry optimizations were carried out with B3LYP functional and the Lanl2DZ/6-31G(d,p) basis sets were used for Cu/other atoms. Single point calculations were performed with the dispersion-corrected M06 functional and the SDD/6-311++G(d,p) Cu/other atoms. The SMD solvent model with the parameters for pyridine was used to account for solvent effects. Please see Supporting Information for more details.

10.1002/adsc.201700462

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Synthesis of 1-Vinyl/Aryl Benzotriazole 3-Oxides though Copper-Catalyzed C-N Bond Coupling Reaction

Adv. Synth. Catal. **Year**, *Volume*, Page – Page

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